

Amendments to the Claims


Claims 2-15 and 18, 19, 29, and 30 are deleted without prejudice. Claims 1, 16, 17, 27, and 28 are amended. New claims 31-40 are added.

This amendment adds, changes, and/or deletes claims in this application. A detailed listing is presented of all claims that are or were in this application, irrespective of whether the claims remain under examination. The text of all claims under examination appears below, and all claims are presented with an appropriate, defined status-identifier. The amendments to the claims are fully supported throughout the specification.

Detailed and Complete Listing of Claims:

Claim 1: (currently amended) A method of identifying a framework protein for subsequent engineering including the steps of: -

(i) creating a computer database which includes a plurality of entries, each said entry corresponding to a description of a location and orientation in 3D space of side chains of amino acid residues of a framework protein which comprises 70 amino acids or less and has 1-11 disulfide bonds, wherein the location and orientation of each side chain is simplified as a $C\alpha$ - $C\beta$ vector;

 (ii) creating a query corresponding to a description of a location and orientation in 3D space of respective side chains of two or more amino acid residues of a sample protein which are required for a function of said sample protein, wherein the location and orientation of each side chain is simplified as a $C\alpha$ - $C\beta$ vector; and

(iii) searching said database with said query to thereby identify one or more hits wherein at least one of said hits corresponds to a respective said framework protein which has structural similarity to said sample protein.

Claims 2-7: (withdrawn)

Claims 8-15: (canceled)

Claim 16: (previously amended) The method of Claim 1, wherein at step (iii) the hits are ranked according to structural similarity with said sample protein.

Claim 17: (previously amended) The method of Claim 1, wherein searching at step (iii) includes:

- (a) identification of said hits by clique detection;
- (b) filtering of said hits identified at step (a).

Claims 18-26 (withdrawn)

Claim 27: (previously amended) A computer program for searching a protein database which comprises a plurality of entries, each said entry corresponding to a distance matrix representation of two or more C α -C β vectors, said program including the steps of:

- (i) comparing a query with each said database entry, said query corresponding to a distance matrix representation of two or more C α -C β vectors; and
- (ii) identifying hits by clique detection, wherein a hit is defined according to a minimum number of C α -C β vector matches between said query and each said entry.

Claim 28: (previously amended) A computer program which filters said hits identified at step (ii) of Claim 27.

Claims 29-30 (withdrawn)

Claim 31: (new) A method of protein engineering including the steps of: -

- (i) creating a computer database which includes a plurality of entries, each said entry corresponding to a description of a location and orientation in 3D space of side chains of amino acid residues of a framework protein which comprises 70 amino acids or less and has 1-11 disulfide bonds, wherein the location and orientation of each side chain is simplified as a C α -C β vector;
- (ii) creating a query corresponding to a description of a location and orientation in 3D space of respective side chains of two or more amino acid residues of a sample protein which are required for a function of said sample protein, wherein the location and orientation of each side chain is simplified as a C α -C β vector;
- (iii) searching said database with said query to thereby identify one or more hits wherein at least one of said hits corresponds to a respective said framework protein which has structural similarity to said sample protein; and
- (iv) modifying an amino acid sequence of said framework protein which corresponds to a hit, by substituting at least one amino acid residue thereof with at least one

amino acid residue of said sample protein to thereby create an engineered framework protein having increased structural similarity to said sample protein.

Claim 32: (new) The method of Claim 31, wherein the at least one of the amino acid residues of said sample protein represent at least a portion of at least one functional region of said sample protein.

Claim 33: (new) The method of Claim 31, wherein at least two of the amino acid residues of said sample protein which substitute amino acid residues of said framework protein are non-contiguous in primary sequence.

Claim 34: (new) The method of Claim 31, further including the step of determining whether the engineered framework protein has greater stability than said sample protein.

Claim 35: (new) The method of claim 31, further including the step of determining whether the engineered framework protein has increased structural similarity compared to said sample protein.

Claim 36: (new) The method of claim 31, further including the step of determining whether the engineered framework protein exhibits a function which is similar to or inhibitory of, a function of said sample protein.

Claim 37: (new) The method of Claim 31, wherein the sample protein is a cytokine.

Claim 38: (new) The method of Claim 37, wherein the cytokine is selected from the group consisting of GH, IL-4, IL-6, and G-CSF.

Claim 39 (new) The method of claim 1, wherein said query of step (ii) is a single query.

Claim 40 (new) The method of claim 31, wherein said query of step (ii) is a single query.